REMARKS

To simplify the issues in this case, Applicants have canceled claims 1-13 and 15-64 directed to compositions and methods of treatment. Claims 1-13 and 15-64 have been canceled without prejudice so that the subject matter of these claims may be pursued in a future application. New claims 73-119 have been added. Applicants respectfully submit that new claims 73-119 do not represent new matter as the subject matter of these new claims is similar to the subject matter of the canceled dependent composition claims. Claims 65-119, directed to methods of preparation, are pending.

REJECTION UNDER 35 U.S.C. § 103(a):

In the Advisory Action, the Examiner maintained his rejections from the Final Office Action mailed July 3, 2002 of claims 1-17, 21-25, 32-44, 61-67 and 69-72 under 35 U.S.C. § 103(a) as being unpatentable over the '359 patent in view of the '865 patent and of claims 1-72 under 35 U.S.C. § 103(a) as being unpatentable over the '359 patent in view of the '865 patent and further in view of the '574 patent.

To simplify the issues in this case and thereby expedite prosecution, Applicants have canceled composition claims 1-13, 15-64, without prejudice. With regard to the pending process claims, Applicants respectfully disagree with the Examiner for the reasons set forth below.

Independent method claim 65 of the present invention recites, in pertinent part:

> a method of preparing a bioavailable sustained release oral solid dosage form... comprising:
>
> a) preparing a sustained release granulate comprising a gelling agent, said gelling agent comprising a heteropolysaccharide gum and a homopolysaccharide gum capable of cross-linking said heteropolysaccharide gum when exposed to an environmental fluid; **thereafter**
>
> b) **adding** to said sustained release granulate a therapeutically

> effective amount of a medicament having a solubility of more than about 10 g/l **and a pH modifying agent** comprising an organic acid that facilitates the release of said medicament from said dosage form to form a mixture; ....

The '359 patent cited by the Examiner is directed to a sustained release matrix comprising a gelling agent, a cationic cross-linking agent and an inert diluent (See: col 4, lines 33-38). The cationic cross-linking agents described in the '359 patent do not include organic acids and the '359 patent does not otherwise teach, hint or suggest the use of organic acids. As such, the '359 patent cannot possibly teach or suggest the addition of an organic acid pH modifying agent and an active medicament to an already pre-formed sustained release granulate as claimed in independent claim 65 of the present invention.

The '865 patent is directed to a "ready to use" sustained release excipient comprising a homopolysaccharide (e.g., locust bean gum) with an ionizable gel strength enhancing agent (e.g., organic acid) and an inert diluent (See: '865 patent page 10, lines 14-19 and Examples 1-3, Table 1). The '865 patent is cited by the Examiner for its "teaching equivalence of organic acids with cationic cross-linking agents of the '359 patent." However, the organic acids of the '865 patent are gel strength enhancing agents which are part of the sustained release excipient. The organic acids of the '865 patent provide increased gel strength when the homopolysaccharide is exposed to an aqueous environment, thus preventing an initial "burst" of active medicament release from the formulation.

This is very different from present method claim 65, wherein a ph modifying agent (i.e. an organic acid) and an active medicament are added to an already formed excipient (i.e. the sustained release granulate) to facilitate the release of medicament from a dosage form. Combining the '359 and '865 patents would not lead one skilled in the art to the present invention, as both the cationic cross-linking agents of both the '359 patent and the '865 patent are incorporated into the sustained release excipient. Combining these references would clearly lead one skilled in the art to again

incorporate the cationic cross-linking agent (e.g. organic acid of the '865 patent) into the excipient.

In his final Office Action, the Examiner asserted that "whether the organic acid is added to the heteropolysaccharide /homopolysaccharide gum blend or with a medicament does not appear to be critical. Either way results in a mixture of the heteropolysaccharide gum, medicament, and organic acid."

However, when determining the patentability of process claims, the steps of the process are critical. Further, the difference in whether the organic acid is part of the excipient or is added with medicament to the excipient is critical to how the organic acid functions in the sustained release formulation. In the '865 patent, the result is prevention of initial burst of active medicament from the formulation. In Claim 65 of the present invention, addition of the organic acid and medicament to the excipient results in facilitation of release of medicament from the dosage form.

Finally, the Examiner argued in his Advisory Action that the claims "do not state any particular manner in which the release is facilitated and '865 teaches that the sustained release of the medicament is facilitated by the inclusion of the organic acid." Contrary to the Examiner's assertion, and as previously explained in Applicant's Amendment filed on November 1, 2002, the organic acid cross-linking agent of the '865 patent does not "facilitate" the release of the medicament from the dosage form as asserted by the Examiner. It also does not facilitate the release from the sustained release formulation. It must be reiterated that the organic acids of the '865 patent are gel strength enhancing agents providing increased gel strength when the homopolysaccharide is exposed to an aqueous environment, thus preventing an initial "burst" of active medicament release from the formulation. One skilled in the art reviewing both the '865 patent and the present invention would understand that an organic acid that facilitates the release of active medicament from a formulation is functioning very differently from an organic acid that prevents an initial burst of active medicament from a formulation.

In view of the above, independent method claim 65 of the present invention is not obvious over the '359 patent in view of the '865 patent. As claims 66-72 and new claims 73-85, 88-90 and 97-107 depend from claim 65, these claims are also not obvious over the '359 patent in view of the '865 patent. It should also be noted tat former claims 19-20, 26-31, 45 and 49-59 were not rejected over the '359 patent in view of the '865 patent. As new claims 86-87, 91-96, and 108-119 correspond to former claims 19-20, 26-31, 45 and 49-59, respectively, these claims also should not be rejected over the '359 patent in view of the '865 patent.

The '574 patent "teaches inclusion of a surfactant in xanthan gum/locust bean gum composition provides a bimodal or multi-phase controlled release of a therapeutically active ingredient...such xanthan gum/locust bean gum compositions are effective for delivering active agents such as diltiazem." Combination of the '574 reference with the '359 and '865 patents does not bring one skilled in the art any closer to the present invention. Indeed, the '574 patent only teaches inclusion of a surfactant for provision of bimodal or multi-phase controlled release. It does not teach or suggest inclusion of an organic acid to provide facilitated release. Therefore, the addition of this reference adds nothing to the teachings of the '359 and '865 patents regarding use of organic acids.

Accordingly, independent method claim 65 of the present invention is not obvious over the '359 patent in view of the '865 patent and further in view of the '574 patent. As claims 66-119 depend from claim 65, these claims are also not obvious over the '359 patent in view of the '865 patent and further in view of the '574 patent. Therefore, Applicants respectfully request that the Examiner's § 103(a) rejections be removed.

CONCLUSION

Applicants respectfully submit that in view of the arguments made, the pending claims are in condition for allowance. An early and favorable action on the merits is earnestly solicited.

This Amendment is being filed together with a Request for Continued Examination (RCE). A check in the amount of $860.00 is enclosed, $750.00 of which is for the RCE fee and $110.00 of which is for the petition for a one-month extension of time. If it is determined that any additional fees are due or that any fees have been overpaid, the Commissioner for Patents is hereby authorized to charge said fees or credit any overpayment to Deposit Account No. 50-0552.

Respectfully submitted,

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